Smith-Magenis syndrome

Smith-Magenis syndrome is a developmental disorder that affects many parts of the body. The major features of this condition include mild to moderate intellectual disability, delayed speech and language skills, distinctive facial features, sleep disturbances, and behavioral problems.

Most people with Smith-Magenis syndrome have a broad, square-shaped face with deep-set eyes, full cheeks, and a prominent lower jaw. The middle of the face and the bridge of the nose often appear flattened. The mouth tends to turn downward with a full, outward-curving upper lip. These facial differences can be subtle in early childhood, but they usually become more distinctive in later childhood and adulthood. Dental abnormalities are also common in affected individuals.

Disrupted sleep patterns are characteristic of Smith-Magenis syndrome, typically beginning early in life. Affected people may be very sleepy during the day, but they have trouble falling asleep and awaken several times each night.

People with Smith-Magenis syndrome have affectionate, engaging personalities, but most also have behavioral problems. These include frequent temper tantrums and outbursts, aggression, anxiety, impulsiveness, and difficulty paying attention. Self-injury, including biting, hitting, head banging, and skin picking, is very common. Repetitive self-hugging is a behavioral trait that may be unique to Smith-Magenis syndrome. People with this condition also compulsively lick their fingers and flip pages of books and magazines (a behavior known as "lick and flip").

Other signs and symptoms of Smith-Magenis syndrome include short stature, abnormal curvature of the spine (scoliosis), reduced sensitivity to pain and temperature, and a hoarse voice. Some people with this disorder have ear abnormalities that lead to hearing loss. Affected individuals may have eye abnormalities that cause nearsightedness (myopia) and other vision problems. Although less common, heart and kidney defects also have been reported in people with Smith-Magenis syndrome.

Frequency

Smith-Magenis syndrome affects at least 1 in 25,000 individuals worldwide. Researchers believe that many people with this condition are not diagnosed, however, so the true prevalence may be closer to 1 in 15,000 individuals.

Genetic Changes

Most people with Smith-Magenis syndrome have a deletion of genetic material from a specific region of chromosome 17. Although this region contains multiple

genes, researchers believe that the loss of one particular gene, *RAI1*, in each cell is responsible for most of the characteristic features of this condition. The loss of other genes in the deleted region may help explain why the features of Smith-Magenis syndrome vary among affected individuals.

A small percentage of people with Smith-Magenis syndrome have a mutation in the *RAI1* gene instead of a chromosomal deletion. Although these individuals have many of the major features of the condition, they are less likely than people with a chromosomal deletion to have short stature, hearing loss, and heart or kidney abnormalities.

The *RAI1* gene provides instructions for making a protein whose function is unknown. Mutations in one copy of this gene lead to the production of a nonfunctional version of the RAI1 protein or reduce the amount of this protein that is produced in cells. Researchers are uncertain how changes in this protein result in the physical, mental, and behavioral problems associated with Smith-Magenis syndrome.

Inheritance Pattern

Smith-Magenis syndrome is typically not inherited. This condition usually results from a genetic change that occurs during the formation of reproductive cells (eggs or sperm) or in early fetal development. Most often, people with Smith-Magenis syndrome have no history of the condition in their family.

Other Names for This Condition

- 17p- syndrome
- 17p11.2 monosomy
- chromosome 17p deletion syndrome
- deletion 17p syndrome
- partial monosomy 17p
- SMS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Smith-Magenis syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0795864/

Other Diagnosis and Management Resources

- GeneReview: Smith-Magenis Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1310
- MedlinePlus Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Health Topic: Brain Malformations
  https://medlineplus.gov/brainmalformations.html
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html

Genetic and Rare Diseases Information Center

- Smith-Magenis syndrome
  https://rarediseases.info.nih.gov/diseases/8197/smith-magenis-syndrome

Educational Resources

- Disease InfoSearch: Smith-Magenis syndrome
  http://www.diseaseinfosearch.org/Smith-Magenis+syndrome/6651
- MalaCards: smith-magenis syndrome
  http://www.malacards.org/card/smith_magenis_syndrome
- Orphanet: Smith-Magenis syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=819

Patient Support and Advocacy Resources

- Chromosome Disorder Outreach
  http://chromodisorder.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/smith-magenis-syndrome/

- PRISMS: Parents and Researchers Interested in Smith-Magenis Syndrome
  http://www.prisms.org/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/smith-ma.html

GeneReviews

- Smith-Magenis Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1310

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22smith-magenis+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Abnormalities,+Multiple%5BMAJR%5D%29+AND+%28smith-magenis+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- SMITH-MAGENIS SYNDROME
  http://omim.org/entry/182290

Sources for This Summary

- Elsea SH, Williams SR. Smith-Magenis syndrome: haploinsufficiency of RAI1 results in altered gene regulation in neurological and metabolic pathways. Expert Rev Mol Med. 2011 Apr 19;13:e14. doi: 10.1017/S1462399411001827. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21545756
- GeneReview: Smith-Magenis Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1310
- Girirajan S, Elsas LJ 2nd, Devriendt K, Elsea SH. RAI1 variations in Smith-Magenis syndrome patients without 17p11.2 deletions. J Med Genet. 2005 Nov;42(11):820-8. Epub 2005 Mar 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15788730
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735950/
- Girirajan S, Vlangos CN, Szomju BB, Edelman E, Trevors CD, Dupuis L, Nezarati M, Bunyan DJ, Elsea SH. Genotype-phenotype correlation in Smith-Magenis syndrome: evidence that multiple genes in 17p11.2 contribute to the clinical spectrum. Genet Med. 2006 Jul;8(7):417-27.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16845274
- Gropman AL, Duncan WC, Smith AC. Neurologic and developmental features of the Smith-Magenis syndrome (del 17p11.2). Pediatr Neurol. 2006 May;34(5):337-50. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16647992

- Martin SC, Wolters PL, Smith AC. Adaptive and maladaptive behavior in children with Smith-Magenis Syndrome. J Autism Dev Disord. 2006 May;36(4):541-52.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16570214
- Shelley BP, Robertson MM. The neuropsychiatry and multisystem features of the Smith-Magenis syndrome: a review. J Neuropsychiatry Clin Neurosci. 2005 Winter;17(1):91-7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15746488
- Smith AC, Dykens E, Greenberg F. Behavioral phenotype of Smith-Magenis syndrome (del 17p11.2). Am J Med Genet. 1998 Mar 28;81(2):179-85. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9613859
- Tomona N, Smith AC, Guadagnini JP, Hart TC. Craniofacial and dental phenotype of Smith-Magenis syndrome. Am J Med Genet A. 2006 Dec 1;140(23):2556-61.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17001665

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